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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/752,292	12/28/2000	Alex Chenchik	CLON-017US2	6642

24353 7590 08/12/2003

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EXAMINER
ZITOMER, STEPHANIE W

ART UNIT	PAPER NUMBER
1634	

DATE MAILED: 08/12/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/752,292	CHENCHIK ET AL.	
	Examiner	Art Unit	
	Stephanie Zitomer	1634	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *27 January 2003* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,4-10,12,13,15,16,18-22 and 24* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,4-10,12,13,15,16,18-22 and 24* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Application status

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on January 27, 2003 has been entered.

2. Rejections not reiterated herein from the Final Office Action mailed June 19, 2002 have been withdrawn. Applicant's remarks and arguments have been fully considered. Arguments to withdrawn rejections are deemed moot.

3. The Terminal Disclaimer filed January 27, 2003 has been accepted and has obviated the provisional rejection over the related application, serial no. 09/792,293.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Rejection under 35 U.S.C. 112, second paragraph: Indefiniteness

4. Claims 1, 4-10, 12, 13, 15, 16, 18-22 and 24 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

(a) The claims lack antecedent basis for "tag complements" and "hybridization" in all claims in which these terms appear because there is no recitation or indication that the tags are hybridizable. It is suggested to clarify that the tags are nucleic acids.

(b) Claims 1, 4-10, 12, 13, 15, 16 and 18-21 lack antecedent basis for "location" because there is no recitation or indication that the tag complements have "locations" in the array. It is suggested to clarify by amening claim 1 to show that arrays have "locations".

(c) Claims 4-9 lack antecedent basis in claim 1 for "any two tag-tag complement pairs" because claim 1 recites "at least one" tagged affinity ligand and "at least one" hybridization complex. It is suggested to provide appropriate antecedent basis in claim 1.

Rejection under 35 U.S.C. 102(b): Anticipation

5. Claim 1 is rejected under 35 U.S.C. 102(b) as being anticipated by the patent to Brenner (5,863,722 issued January 26, 1999). Brenner discloses the claimed method of detecting at least one analyte in a sample comprising (a) forming a population of complexed analyte/tagged affinity ligands wherein the tag is an oligonucleotide (nucleic acid); (b) capturing the complexes on a solid support by hybridizing the tags with tag complements attached to the solid support wherein the tag complements have specific locations in the array (column 2, line 66-column 3, line 11); and (c) detecting the presence of at least one analyte in the sample from the presence and location of at least one surface bound hybridization complex (column 3, lines 61-65; column 19, lines 20-49).

Rejections under 35 U.S.C. 103(a): Obviousness

6. Claims 4-9 are rejected under 35 U.S.C. 103(a) as being unpatentable over Brenner as applied to claim 1 above (paragraph 4) and further in view of Shannon et al. (6251,588) and Lockhart et al. (6,333,155). The claim 1 method embodiments of claims 4-9 differ from that of Brenner wherein any difference in hybridization efficiency between any two tag/tag complements does not exceed about 10 fold (claim 4), about 5 fold (claim 5) or about 3 fold (claim 6) and wherein the level of cross-hybridization of any tag employed in the method does not exceed about 10% (claim 7), about 2% (claim 8) or about 1% (claim 9). However, the practice of optimizing hybridization efficiency and reducing background by minimizing cross-hybridization in the use of nucleic acid arrays was routine in the art at the time the claimed invention was made. For example, Shannon et al. provide a description of the prior art on the topic as well the rationale for optimizing hybridization efficiency of oligonucleotides in arrays (column 2, line 52-column 6, line 19). Lockhart et al. address the need for optimizing the hybridization efficiency of oligonucleotides in an array as

well as the problem of cross-hybridization: "it is recognized that hybridization efficiency varies with base composition and probe length" (column 14, lines 63-64) and "oligonucleotide probes in the high density array are selected to bind specifically to the nucleic acid target to which they are directed with minimal non-specific binding or cross-hybridization" (column 15, lines 64-67). Furthermore, Brenner discusses the cross-hybridization problem at length and presents an algorithm for determining minimally cross-hybridizing nucleotide sets (column 6, line 13-column 7, line 45). Therefore, it would have been obvious and the skilled practitioner in the art at the time the claimed invention was made would have been motivated to select tag/tag complements having hybridization efficiencies with minimal differences and minimal cross-hybridization for the known benefits of minimizing interferences and maximizing hybridization results. In *In re Aller*, 105 USPQ 233, the court found that changes of an old process within the broad teaching of the prior art does not impart patentability in the absence of unexpected results.

7. Claims 10, 12, 13 and 15 are rejected under 35 U.S.C. 103(a) as being unpatentable over Burmer (6,087,103 filed March 4, 1998 further in view of Brenner (as above, paragraph 5). The claims are drawn to the assay method of claim 1 for detecting at least one analyte in a sample comprising (a) forming a population of complexed analyte/tagged affinity ligands wherein the tag is an oligonucleotide (nucleic acid); (b) capturing the complexes on a solid support by hybridizing the tags with tag complements attached to the solid support wherein the tag complements have specific locations in the array and (c) detecting the presence of at least one analyte in the sample from the presence and location of at least one surface bound hybridization complex (column 3, lines 61-65; column 19, lines 20-49). Burmer discloses a method of detecting the presence of at least one analyte in a sample comprising contacting the sample with a population of tagged affinity ligands wherein the analytes are polypeptides or proteins and the ligand is an antibody (column 4, lines 66-67; column 7, lines 14-19). The claimed invention method embodiments of claims 10, 12 and 15 differ from the method of Burma wherein the tags are hybridized to tag complements in an

array whereas Burma hybridizes the tags to an array for identification after they have been separated from the ligands. However, Brenner teachs hybridization of tagged ligands to an array of tag complements (column 2, line 66-column 3, line 11; column 3, lines 45-65). It would have been obvious and the skilled practitioner in the art would have been motivated at the time the claimed invention was made to hybridize the attached tag of the tagged antibody ligand and polypeptide analyte of Burmer to the tag complements in the array for the obvious benefit of eliminating the time consuming step of removing the tag and separately hybridizing it to the tag array for identification. Regarding claim 13 wherein the tagged affinity ligands are labeled, Burmer teaches this embodiment (column 13, lines 7-8).

8. Claims 16, 18-22 and 24 are rejected under 35 U.S.C. 103(a) as being unpatentable over Brenner as applied to claim 1 above (paragraph 5) in view of Lockhart and Shannon, cited above (paragraph 6), Burmer, cited above (paragraph 7), and further in view of Brown et al. (Nat. Gen. Suppl. 21:33-37, Jan. 1999). Regarding claim 16, the claimed invention differs from Brenner wherein the array of distinct tag complements immobilized on a solid support, a set of affinity ligands comprising tags that hybridize to tag complements on the array and means for detecting the location of hybridized tag/tag complements comprise a kit. Brenner discloses the array of distinct tag complements on a solid support having spatially discrete regions (column 2, line 66-column 3, line11, a set of distinct tagged affinity ligands (column 3, lines 24-38). The claimed invention differs from Brenner wherein these reagents comprise a kit. However, Burmer teaches a kit comprising similar reagents (column 15, lines 9-13). It would have been obvious and the skilled practitioner in the art would have been motivated to provide the reagents disclosed in Brenner in kit form as taught by Burmer for the known benefits of convenient use and commercial application.

Regarding claim 22, the claimed array of distinct tag complements wherein at least one is hybridized to a tagged affinity ligand is disclosed by Brenner (column 3, lines 47-60).

Regarding claims 18, 19 and 22, the kit and array embodiments differ from Brenner in view of Burmer wherein the magnitude of difference in hybridization efficiency between any two tag/tag complement pairs does not exceed about 10 fold and any tag in the set of tagged affinity ligands has a level of cross-hybridization with respect to the array that does not exceed 10%. However, the practice of optimizing hybridization efficiency and minimizing cross-hybridization in the use of nucleic acid arrays was routine in the art at the time the claimed invention was made. For example, Shannon et al. provide a description of the prior art on the topic as well the rationale for optimizing hybridization efficiency of oligonucleotides in arrays (column 2, line 52-column 6, line 19). Lockhart et al. address the need for optimizing the hybridization efficiency of oligonucleotides in an array as well as the problem of cross-hybridization: "it is recognized that hybridization efficiency varies with base composition and probe length" (column 14, lines 63-64) and "oligonucleotide probes in the high density array are selected to bind specifically to the nucleic acid target to which they are directed with minimal non-specific binding or cross-hybridization" (column 15, lines 64-67). Brenner addresses the cross-hybridization problem at length and presents an algorithm for determining minimally cross-hybridizing nucleotide sets (column 6, line 13-column 7, line 45). Therefore, it would have been obvious and the skilled practitioner in the art at the time the claimed invention was made would have been motivated to select tag/tag complements having hybridization efficiencies with minimal differences and minimal cross-hybridization for the known benefit of maximizing hybridization results. In *In re Aller*, 105 USPQ 233, the court found that changes of an old process within the broad teaching of the prior art does not impart patentability in the absence of unexpected results.

Regarding claims 20 and 21, the claimed invention kit differs from that of Brenner in view of Burmer wherein the means for identifying the physical location on the array comprises a medium that includes identifying information or a means for remotely assessing the information is provided in the kit wherein the latter is a website address. However, it would have been obvious and the

skilled practitioner in the art would have been motivated at the time the claimed invention was made to include printed information such as a website address in the kit in view of routine practice in the art of accessing public nucleotide sequence databases for sequence searching for the obvious benefit of obtaining a large amount of sequence information in a readily available format. For example, Brown et al. teach that the use of molecular arrays generates a large amount of information which may be managed and published via websites. Brenner teaches that data are collected by computer where it can be stored, viewed and analyzed (column 20, lines 21-23). Obviously, large amounts of such data would be appropriately provided in a website.

Regarding claim 24, the claimed invention array differs from that of Brenner wherein the array has a density that does not exceed about 400 spots/square cm. However, oligonucleotide arrays routinely used in the prior art were known to have densities ranging from less than 100 to more than 1000 spots per square cm. Therefore, one of ordinary skill in the art at the time the claimed invention was made would have been motivated according to personal preference to select an array density appropriate to particular experimental parameters for the obvious benefit of optimizing results.

Response to applicant's arguments

9. Applicant's arguments filed January 27, 2003 have been fully considered but they are not persuasive. It is alleged that Brenner does not teach identifying the analyte in the complex by "relating information about the location of a complex on a substrate surface to the identity of the analyte in the complex at that location". In response to applicant's argument that the references fail to show certain features of applicant's invention, it is noted that the features upon which applicant relies (i.e., "identity of the analyte)) are not recited in the rejected claims. Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993). Claim 1 recites that the presence of the analyte is identified.

Conclusion

10. No claim is allowed.

11. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Stephanie Zitomer whose telephone number is (703) 308-3985. The examiner can normally be reached on Monday through Friday from 10:00 am to 4:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, W. Gary Jones, can be reached on (703) 308-1152. The official fax phone number for this Group is (703) 308-4242. The unofficial fax number is (703) 308-8724. The examiner's Rightfax number is 703-746-3148.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196. For questions and requests relating to formal matters contact LIE Chantae Dessau at 703-605-1237.

Stephanie Zitomer, Ph.D.
August 11, 2003

STEPHANIE ~~W.~~ ZITOMER
PRIMARY EXAMINER